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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/015,532	12/11/2001	Julio C. Medina	11134-005-999	4305

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EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	13

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SM 1

Office Action Summary	Application No.	Applicant(s)	
	10/015,532	MEDINA ET AL.	
	Examin r	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *136-204* is/are pending in the application.

4a) Of the above claim(s) *160,161,171,172,191,192 and 198-201* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *136-159,162-170,173-190,193-197 and 202-204* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 March 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,7,8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. This action is in response to an application filed on 3/13/03. There are fifty-nine claims pending and forty-nine under consideration. Claims 136-152 are compound claims. Claim 153 is a composition claim. Claims 154-159, 162-170, 173-190, 193-197, and 202-204 are use claims. This is the first action on the merits. The application concerns some pyrido[2,3-d]pyrimidine compounds, compositions, and uses thereof.

Election/Restrictions

2. Applicant's election with traverse of Group I in Paper No. 12 is acknowledged. The traversal is on the ground(s) that no restriction within a claim is allowed and that the previously made restriction amounts to a rejection. Applicants cite *In re Haas* 179, USPQ 623, *In re Haas* 198 USPQ 334, and *In re Weber* 198 USPQ 331 in support of the latter assertion. This is not found persuasive because firstly, there can be no doubt of the USPTO's ability to restrict within a claim. The MPEP § 803.02 provides the guidance of the procedure to use when restricting within a single Markush-type claim like Applicants, "[b]roadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility." In the present case, the heterocyclic core clearly has different structural features and is not, by itself, responsible for the claimed

therapeutic activity. The art applied below is much closer to some of the claimed compounds than the claimed compounds are, in turn, to each other. Secondly, all the cases cited by Applicants deal with a rejection of claims under 35 USC 121 and not on the ability of the USPTO to restrict an application. Until now, no claims have been rejected. The requirement is still deemed proper and is therefore made FINAL.

3. In the written restriction requirement, the Examiner indicated that claim 161 linked Groups I and II. This is erroneous. Claim 161 depends upon claim 160, which is part of group III alone. The Examiner regrets the error.

4. Claims 160, 161, 171, 172, 191, 192, and 198-202 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in Paper No. 12.

5. Objection is made to claims 136, 138, 140-159, 162-170, 187-190, 193-197, and 202-204 as containing non-elected subject matter. The claimed compounds, compositions, and methods that employ them present a variable core. Formula of claim 136 contains compounds drawn to the non-elected inventions to the extent it reads upon compounds with X = a bond.

Title

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed after restriction. The following title is suggested: addition of the word "Pyrido[2,3-d]pyrimidine" to the beginning of the title.

Abstract

7. Applicant is reminded of the proper content of an abstract of the disclosure. A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." The abstract is too short and generic. Examiner suggests claim 136, lines 1-5 including the figure, and the utility.

Priority

8. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional applications upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 136-159, 162-179, 174-190, 193-197, and 202-204 of this application. Provisional Application 60/255,241 is drawn to quinazoline compounds. While it is possible that the heteroaryl ring formed by two R^{12} radical could include pyridine, as

required by the present claim 136, there is nothing pointing to this possibility. In fact, Claim 50 does not mention the pyrido[2,3-d]pyrimidine bicyclic ring of the present Application. Claims 51-61 of Provisional Application 60/255,241 point to quinazoline compounds and away from the presently claimed subject mater.

9. Claim 51 of Provisional Application 60/296, 499 does teach that variable X can be C(O) or CH_2 but the figures on page 14 of Provisional Application 60/296, 499 include the presently claimed 4-one compounds but exclude the presently claimed 4-dihydro compounds. In addition claim 62 of Provisional Application 60/296, 499 also teaches away from this possibility. The definitions of A^4, $R^{3,}$ and R^{14} also differ between claim 51 of Provisional Application 60/296, 499 and claim 136 of the present application.

Claim Objections

10. Objection is made to claim 189 under 37 CFR 1.75 as being a duplicate of claim 161. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Both claims are drawn to the treatment of two specific diseases with the same set of compounds.

11. Claims 156, 157, 170, and 190 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a

previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In lines 2-8, page 13, 9-14, page 18, and 2-4, page 19 Applicants state that all compounds of the formula of claim 136 are antagonists of CXCR3. Thus, there are no compounds of claim 136 excluded in these four claims. In the alternative, if Applicants are aware of any compounds of the claimed formula that are not antagonists of this chemokine, then please inform the Examiner so that the proper utility rejection may be made.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 136-159, 162-170, 173-190, 193-197, and 202-204 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The word "prodrug" is indefinite. The issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' "prodrugs" are molecules whose structure lie outside the subject matter of the formula of claim 136, but upon metabolism in the body are converted to active compounds falling within the structural scope of that formula. The claim describes the function

intended but provides no specific structural guidance to what constitutes a "prodrug". Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claim 136. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise. Applicants define the concept of prodrug in the passage spanning line 20, page 11 to line 2, page 12. "Ester" prodrugs are exemplified but it is unclear if these are esters of claimed acids or esters of claimed alcohols. It is also unclear what reagents are used to makes these esters. Are only alkyl alcohols to be used, for example, or are there any limits?

The Examiner suggests deleting "prodrug".

13. Claims 193 and 194 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Both claims recite the limitation "said organ transplant condition" in line 1. There is insufficient antecedent basis for this limitation in the parent claim 187 that does not mention organ transplants.

14. Claims 187, 190, and 202 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The specification does not set forth any steps involved in determining how to identify

"a CXCR3-mediated condition or disease". It is unclear what diseases and treatments applicant is intending to encompass. Applicants define the phrase in lines 3-20, page 25 but repeatedly indulge in speculation, "might" "may be". The passage spanning line 26, page 25 to line 30, page 26 lists a number of disease conditions without clarify if these diseases are related to CXCR3. Are all infections, for example CXCR3-related diseases? Determining whether a given disease responds or does not respond to such a chemokine antagonist and thus, covered by the claim language, will require extensive and potentially inconclusive clinical research. With out such clinical research to identify the patients and diseases Applicants intend to treat, the physician skilled in the clinical arts cannot determine the metes and bounds of the claim. Hence, the claims are indefinite.

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 136-159, 162-179, 174-190, 193-197, and 202-204 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for salts of the claimed compounds, does not reasonably provide enablement for prodrugs of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make or use the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, that produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism *de novo*, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active. Determining whether a particular compound meets these three criteria in a clinical trial setting requires a large degree of experimentation.

b) The direction concerning making the prodrugs is found in the paragraph spanning line 20, page 11 to line 2, page 12. c) There is no working example of a prodrug of a compound the formula of claim 136. d) The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the human body. e) The state of the prodrug art is summarized by Wolff (Medicinal Chemistry). The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modern Pharmaceutics) in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug. f) Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. g) The lack of predictability in finding prodrugs was discussed above. h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula of claim

136 as well as the presently unknown list potential prodrug derivatives embraced by claim 136.

Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

16. Nowhere in the specification are directions given for preparing the "prodrugs" of the claimed compounds. Since the structures of these "prodrugs" are uncertain, direction for their preparation must be even more unclear. Direction to the pharmacologist for how to search for the claimed prodrugs hardly substitute for directions to the synthetic organic chemist of how to make these compounds.

17. Claims 154-159, 162-170, 173-190, 193-197, and 202-204 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for treating any human disease. The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above. a) Determining if any particular claimed compound would treat any particular human disease would require synthesis of the compound, formulation into a suitable dosage form, and either subjecting it clinical trials with a number of fundamentally different diseases described below or subjecting it to testing in an art-recognized disease model,

which is correlated to clinical efficacy. This is a large degree of experimentation. b) The direction concerning treating diseases is found in the passage spanning line 30, page 24 to line 30, page 26, which merely states Applicants' intention to do so. Applicants describe no formulations. Possible routes of administration are taught in lines 31, page 26 to line 3, page 27. Possible doses and dosing schedules required to practice their invention are taught in lines 4 to 22, page 27. A 10,000-fold range of dosage is contemplated. Since no CXCR3 antagonist has ever been used to treat any human disease, how the skilled physician to know what dose to administer to her patients? There is a single *in vitro* assay described in the passage spanning line 14, page 162 to line 14, page 163 with no data. Applicants have not asserted and it is not art-recognized that the results of this *in vitro* assay are correlated to clinical efficacy of any disease treatment. There is no art-recognized *in vivo* disease models used to test Applicants' compounds.

c) There is no working example of treatment of any disease in man or animals. d) The nature of the invention is clinical treatment of disease, which involves physiological activity. e) The state of the clinical arts with CXCR3 antagonists is provided by Carter (Curr. Opin. Chem. Biol.) who reports in Table 1, page 512, that mice lacking CXCR3 receptors are normal. In the paragraph spanning pages 513-514 elevated levels of this chemokine are reported in both

psoriasis and MS patients, although no treatment of any such patients by antagonists of this chemokine were known in 2002. Table 3, page 516 makes clear that no CXCR3 antagonists were known in 2002. Thus, logically no diseases treatable by such antagonists could have been found by this date.

Onuffer (TRENDS in Pharm. Sci.) in Table page 460 reports MS, arthritis, sarcoidosis, allograph rejection, and cancer treatment as "possible therapeutic indications". Thus, such treatments were speculative and not established in 2002. Table 2 and Table 3, pages 462 and 463 confirm that no CXCR3 antagonists were in clinical development in 2002. The only complete paragraph in column 2, page 462 reports that CXCR3 was the subject of drug development programs. Thus, in 2002 CXCR3 antagonists were still in the experimental stage and any claims of disease therapy are speculative in nature for which Applicants have provided no empirical support.

Proudfoot (Sem. Immun.) reports in the digram on the top of page 59 that allograph rejecction is the only "target" of CXCR3 ligand research. The first complete paragraph on page 61 states that inhibitors of only two the the fifty chemokine receptos had progessed to clinical trials. Neither of these receptos was CXCR3. The last sentence in the pargarph states "[chemokines] have certainly been a difficult family to work with". Thus, in 2003, two years after Applicants

filing date, only potential targets were art recognized and no therapeutic applications had been identified.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The scope of the claims involves all of the thousands of compounds of claim 136 as well as the hundred of diseases embraced by the term CXCR3 related disease. Thus, the scope of claims is very broad.

Substantiation of use and scope is required when the use is "speculative", "sufficiently unusual", or not provided in the specification, *Ex parte Jovanovics,* 211 USPQ 907, *In re Langer,* 183 USPQ 288, *Hoffman v. Klaus*, 9 USPQ2d 1657, and *Ex parte Powers*, 200 USPQ 925 concerning the type of testing needed to support *in vivo* use claims. Also see the MPEP §2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry. Thus, undue experimentation will be required to determine if any particular claimed compound is, in fact, a treatment of any disease.

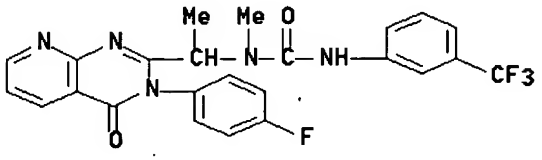
Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 136-139, 142, 143, 145, 147, 149, 153-158, 162, 163, 165, 166, 168, 169, 170, 173, 174, 177, 179, 181, 183, 184, 187, 188, 190, 193-195, 197, and 202-204 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baxter ('005). The reference teaches the compound with registry number 330796-36-6 shown below. The Applicants claim the compounds with n = 0, X = C(O), R^{14} = 4-fluorophenyl, R^1 = methyl, R^2 = hydrogen, and Q = C(O). The reference teaches such a compound with L-R^3 = methyl and R^4 = 3-(trifluoromethyl)phenyl-NH-. Applicants claim the compounds with L-R^3 = alkylene-heteroaryl and R^4 = 3-(trifluoromethyl)phenyl. The compound is shown in the reference in lines 18-35, column 80. It is pictured in column 77 and is compound (20). The difference between the claimed and taught compounds is the urea rather than amide linkage to R^4 and the methyl group rather than alkylene-heteroaryl as L-R^3. These deficiencies are taught internally in the reference. Lines 30-31, page 32 teach that Applicants' claimed N-C(O)- linkage can replace urea linkage found in the working

example (20). Alkylene-heteroaryl is taught as one of four possible substituents that would make up the R^8 radical in the reference in lines 50-56, column 30. This R^8 radical corresponds to Applicants L-R^3 radical.



Lines 1-6, column 52 of the reference teach that cancer treatment is an intended use of the compound shown above. Thus, the intended utility is the same as Applicants' and claims 162, 163, 165, 166, 168, 169, 173, 174, 177, 179, 181, 183, and 184 are made obvious. Formulations are taught in lines 7-54, column 52. Thus, claim 153 is made obvious. Treatment of psoriasis is taught in lines 1-15, column 51 of the reference. Thus, claims 154, 155, 158, 187, 188, 195, and 202 are made obvious. Use of the compound discussed above for artificial and embryonic liver transplants is taught in lines 64-67, column 42 of the reference. Thus, claims 193, 194, and 197 are made obvious. The reference is silent as to the ability of the obvious compounds to antagonize CXCR3. However, the discovery of the mechanism of action of an obvious use or the mechanism of action of an obvious compound does not make that use or those compounds patentable. Thus, claims 156, 157, 170, and 190 are made obvious.

19. Claims 136-139, 142, 143, 145, 147, 149, 153-158, 162, 163, 165, 166, 168, 169, 170, 173, 174, 177, 179, 181, 183, 184, 187, 188, 190, 193-195, 197, and 202-204 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baxter (WO 01/19800 A2, Ref AL). The compound taught by this reference was discussed above. It is found in lines 21-29, page 108. Claims 31-39 of the reference are drawn to the compound above and claim 37 provides the direction to replace the taught urea linkage with an amide linkage. Lines 5-8, page 123, claim 31 provide the teaching that alkylene-heteroaryl is one of four possible substituents that would make up the R^8 radical in the reference. Compositions are taught in claims 29 and 30 of the reference. Claims 1-28 of the reference are drawn to inhibiting altered growth states of cells and the meaning this teaching was discussed above.

Double Patenting

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969). A

timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 136-139, 149, 153, 187-190, 193-197, and 202 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 51, 66, 79, 97, and 110 of copending Application No. 10/164,690. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only differences between the present claim 136 and claim 51 of copending Application No. 10/164,690 are the definitions of variables A^4 and R^{14}. In the present application A = nitrogen and R^{14} = aryl or heteroaryl. In Application No. 10/164,690 A = carbon or nitrogen and R^{14} = five specific aromatic radicals. In the present claim 138 radical R^{14} is restricted to the same five radicals. The skilled medicinal chemist would find it routine experimentation to choose nitrogen from a list of two possible atoms to prepare the presently claimed compounds. This is a provisional

obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Allowable Subject Matter

21. The following is a statement of reasons for the indication of allowable subject matter: Applicant's compounds are patentable over WO 01/30768 A and WO 01/16144 A (ref AS and AT). These two references do not teach the pyrido[2,3-d]pyrimidine core of the present claims.

Conclusion

22. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for before final amendments is (703) 872-9306. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

Thomas McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK
May 30, 2003